iron-refractory iron deficiency anemia

Iron-refractory iron deficiency anemia is one of many types of anemia, which is a group of conditions characterized by a shortage of healthy red blood cells. This shortage prevents the blood from carrying an adequate supply of oxygen to the body's tissues.

Iron-refractory iron deficiency anemia results from an inadequate amount (deficiency) of iron in the bloodstream. It is described as "iron-refractory" because the condition is totally resistant (refractory) to treatment with iron given orally and partially resistant to iron given in other ways, such as intravenously (by IV). In people with this form of anemia, red blood cells are abnormally small (microcytic) and pale (hypochromic). The symptoms of iron-refractory iron deficiency anemia can include tiredness (fatigue), weakness, pale skin, and other complications. These symptoms are most pronounced during childhood, although they tend to be mild. Affected individuals usually have normal growth and development.

Frequency

Although iron deficiency anemia is relatively common, the prevalence of the iron-refractory form of the disease is unknown. At least 50 cases have been described in the medical literature. Researchers suspect that iron-refractory iron deficiency anemia is underdiagnosed because affected individuals with very mild symptoms may never come to medical attention.

Genetic Changes

Mutations in the *TMPRSS6* gene cause iron-refractory iron deficiency anemia. This gene provides instructions for making a protein called matriptase-2, which helps regulate iron levels in the body. *TMPRSS6* gene mutations reduce or eliminate functional matriptase-2, which disrupts iron regulation and leads to a shortage of iron in the bloodstream. Iron is an essential component of hemoglobin, which is the molecule in red blood cells that carries oxygen. When not enough iron is available in the bloodstream, less hemoglobin is produced, causing red blood cells to be abnormally small and pale. The abnormal cells cannot carry oxygen effectively to the body's cells and tissues, which leads to fatigue, weakness, and other symptoms of anemia.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- anemia, hypochromic microcytic, with defect in iron metabolism
- IRIDA
- IRIDA syndrome
- iron-handling disorder, hereditary

Diagnosis & Management

These resources address the diagnosis or management of iron-refractory iron deficiency anemia:

- Genetic Testing Registry: Microcytic anemia
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0085576/
- National Heart, Lung, and Blood Institute: How is Anemia Diagnosed?
  https://www.nhlbi.nih.gov/health/health-topics/topics/anemia/diagnosis
- National Heart, Lung, and Blood Institute: How is Anemia Treated?
  https://www.nhlbi.nih.gov/health/health-topics/topics/anemia/treatment

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Anemia
  https://medlineplus.gov/ency/article/000560.htm
- Encyclopedia: Hypochromia
  https://medlineplus.gov/ency/article/003455.htm

- Encyclopedia: Iron Deficiency Anemia
  https://medlineplus.gov/ency/article/000584.htm
- Health Topic: Anemia
  https://medlineplus.gov/anemia.html

Genetic and Rare Diseases Information Center

- Iron-refractory iron deficiency anemia
  https://rarediseases.info.nih.gov/diseases/10957/iron-refractory-iron-deficiency-anemia

Additional NIH Resources

- National Heart, Lung, and Blood Institute: What is Anemia?
  https://www.nhlbi.nih.gov/health/health-topics/topics/anemia/

Educational Resources

- Boston Children's Hospital: Pediatric Anemia
  http://www.childrenshospital.org/conditions-and-treatments/conditions/pediatric-anemia
- Harvard University Information Center for Sickle Cell and Thalassemic Disorders
  http://sickle.bwh.harvard.edu/menu_iron.html
- MalaCards: iron-refractory iron deficiency anemia
  http://www.malacards.org/card/iron_refractory_iron_deficiency_anemia
- Merck Manual Home Health Handbook for Patients & Caregivers: Overview of Anemia
  http://www.merckmanuals.com/home/blood-disorders/anemia/overview-of-anemia
- Orphanet: IRIDA syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=209981

Patient Support and Advocacy Resources

- American Society of Hematology: Patient Groups
  http://www.hematology.org/Patients/Groups.aspx

Genetic Testing Registry

- Microcytic anemia
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0085576/

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22iron-refractory+iron+deficiency+anemia%22+OR+%22IRIDA+syndrome%22

Scientific articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28iron-refractory+iron+deficiency+anemia%5BTIAB%5D%29+OR+%28irida%5BTIAB%5D%29+OR+%28pseudo-iron-deficiency+anemia%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- IRON-REFRACTORY IRON DEFICIENCY ANEMIA
  http://omim.org/entry/206200

Sources for This Summary

- Brissot P, Bardou-Jacquet E, Jouanolle AM, Loréal O. Iron disorders of genetic origin: a changing world. Trends Mol Med. 2011 Dec;17(12):707-13. doi: 10.1016/j.molmed.2011.07.004. Epub 2011 Aug 20. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21862411
- De Falco L, Sanchez M, Silvestri L, Kannengiesser C, Muckenthaler MU, Iolascon A, Gouya L, Camaschella C, Beaumont C. Iron refractory iron deficiency anemia. Haematologica. 2013 Jun; 98(6):845-53. doi: 10.3324/haematol.2012.075515. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23729726
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3669438/
- De Falco L, Totaro F, Nai A, Pagani A, Girelli D, Silvestri L, Piscopo C, Campostrini N, Dufour C, Al Manjomi F, Minkov M, Van Vuurden DG, Feliu A, Kattamis A, Camaschella C, Iolascon A. Novel TMPRSS6 mutations associated with iron-refractory iron deficiency anemia (IRIDA). Hum Mutat. 2010 May;31(5):E1390-405. doi: 10.1002/humu.21243.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20232450
- Finberg KE, Heeney MM, Campagna DR, Aydinok Y, Pearson HA, Hartman KR, Mayo MM, Samuel SM, Strouse JJ, Markianos K, Andrews NC, Fleming MD. Mutations in TMPRSS6 cause iron-refractory iron deficiency anemia (IRIDA). Nat Genet. 2008 May;40(5):569-71. doi: 10.1038/ng.130. Epub 2008 Apr 13.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18408718
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3104019/

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